REMARKS

This Amendment, filed in reply to the Office Action dated April 7, 2010, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 19, 20 and 31-35 are rejected. Claims 36 and 37 are added. Support for the subject matter of Claims 36 and 37 can be found throughout the specification as originally filed, and at, for example, page 101, 1st paragraph, and the paragraph bridging pages 101 and 102. Claim 1 is amended solely to improve clarity.

No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Claims 19, 20, 31, 32 and 35 are Patentable Under 35 U.S.C. § 102(b)

1. On page 2 of the Office Action, Claims 19, 20, 32 and 35 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fleming *et al.* (U.S Patent No. 6,423,501 or WO/98/25647).

In justifying the rejection, the Examiner continues to allege that Fleming *et al.* discloses a method for treating inflammatory diseases, including *inter alia* inflammatory bowel disease, comprising administering an agent that induces CD81-mediated signal transduction, citing column 13, lines 34-45. The Examiner further contends that Fleming *et al.* discloses that such agents "can be anything [that] binds to or interacts with CD81 and induces … or enhances CD81-mediated signal transduction," and may include *inter alia* polyclonal or monoclonal anti-CD81 antibodies, citing column 9, line 65, to column 10, line 3. The Examiner acknowledges that Fleming *et al.* is entirely silent as to the treatment, or improvement, of shortened intestinal

length or diarrhea, however, asserts that because "a compound and all of its properties are inseparable" (citing *In re Papesch*), the anti-CD81 antibody of Fleming *et al.* would inherently treat or improve such symptoms.

In response to Applicants' previous arguments of record, specifically that the rejection is predicated on impermissible picking and choosing, and that Fleming *et al.* does not disclose the presently claimed method with "sufficient specificity" to establish anticipation, the Examiner contends that such arguments are unpersuasive.

First, the Examiner attempts to distinguish *In re Arkley*, 455 F.2d 586 (C.C.P.A 1972) on its facts from the instant rejection, in order to assert that the legal standard set forth in *Arkley* is inapplicable to the instant case. For example, the Examiner asserts that the prior art reference at issue in *Arkley* encompassed "230,000" compounds, but that Fleming *et al.* only discloses 20 diseases "linked by CD81 and the inhibition of inflammatory responses associated with these disorders."

Second, in response to Applicants' arguments that Fleming *et al.* does not qualify as an anticipatory reference because it is not enabling for that which it is cited for, the Examiner asserts that such arguments are unpersuasive because "[Applicants] have not provided persuasive evidence that one skilled in the art would not have accepted that the anti-CD81 antibodies can be used to treat inflammatory responses associated with inflammatory bowel disease."

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully reiterate that Fleming *et al.* does not disclose, either expressly or inherently, the *specific combination* of claim elements claimed by Applicants, *i.e.*, "*arranged as described in the claims*," as anticipation requires. *In re Arkley*, 455 F.2d 586

(C.C.P.A. 1972). To the contrary, Applicants respectfully submit that the selection of the different claim elements from the disclosure of Fleming *et al.* is impermissible; the record lacks *any* reference to any specific embodiment within Fleming *et al.* that unequivocally discloses a method for treating inflammatory bowel disease by administering an antibody against CD81, "arranged as described in the claims." Rather, the rejection is improperly sustained upon the proposition that the disclosure of each claim element *individually* within different passages describing myriad alternatives for each element - with no pattern of preferences to direct those of skill in the art to the claimed combination of claim elements - is sufficient for anticipation. However, nothing in Fleming *et al.* directs those of skill in the art to the specifically claimed method; selection of the presently claimed invention requires the picking and choosing of particular claim elements from broad generic disclosures describing myriad alternatives, which is not the standard for anticipation.

While the Examiner attempts to distinguish *Arkley* on its facts, alleging that *Arkley* is inapplicable because the number of possible embodiments was significantly greater, Applicants respectfully point out that neither the Federal Circuit, *see e.g., Net MoneyIn, Inc. v. Verisign, Inc.*, 2008 U.S. App. LEXIS 21827, 1, 27 (Fed. Cir. 2008), nor the Board of Patent Appeals and Interferences (BPAI), *see e.g., Ex parte Schulze* (Appeal 2009-013421), has confined *Arkley* to its facts.

For example, in *Ex parte Schulze*, substantially less embodiments were at issue vis-à-vis *Arkley*. Nonetheless, the Board stated that:

> there is no dispute that [the prior art reference] teaches, at separate locations throughout the reference, each of the elements of the claims. However, [the prior art reference] **does not teach a single composition with each of the claimed elements**, but requires selection of the

> elements from groups of disclosed compounds … [t]he instant situation is similar to *Arkley* … [t]his picking and choosing is not consistent with an anticipation rejection [emphasis added].

Similarly, from Fleming *et al.*, those of ordinary skill in the art would first need to select a particular agent to target CD81 (*i.e.*, an antibody), then select a specific disease to be treated. Nothing in Fleming *et al.* directs those skill in the art to this combination. At no point does Fleming *et al.* disclose an embodiment containing each of the claimed elements.

Moreover, the instant rejection is further in conflict with the position taken by the Board of Patent Appeals and Interferences in view of *Ex parte Johnson* (Appeal No. 2006-0070) and *Ex parte Vogt* (Appeal No. 2007-3387). In each case, the Board found the anticipation rejections improper because the claim elements had to be individually (and impermissibly) selected from the broad disclosures of the reference patent, where the specification did not *direct* those of ordinary skill in the art to that specific embodiment vis-à-vis the others. Similarly, nothing in Fleming *et al. directs* those of ordinary skill in the art to the combination of elements claimed by Applicants from any other.

It flows from the foregoing that the relied-upon lists in Fleming *et al.*, when used *in combination* (as has been done to make the instant rejection), disclose at best no more than a *genus* of possible treatment methods. While disclosure of a species, if enabled, always anticipates a genus, the converse is not true. *See Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006). Specifically, for a genus to anticipate a species, the law recognizes that the genus must be sufficiently limited, or that a pattern of preferences must exist serving to further narrow the genus to a small number of species, so that one of skill in the art would have "at once envisaged" the species. *See In re Petering*, 301 F.2d 676 (C.C.P.A. 1962). In this regard, Applicants respectfully point out that Fleming *et al.* contemplates a *broad genus* of

possible diseases that can be treated by its inhibition, or by its activation, and a *broad genus* of agents for effecting such. There is no pattern of preferences in Fleming *et al.* that serve to narrow the genus of possible treatment methods to disclose the presently claimed invention with sufficient specificity, as anticipation requires.

Accordingly, Applicants respectfully submit that the rejection is improper not only in view of the *Arkley* line of cases, but also in view of relevant law pertaining to anticipation of a species by a genus.

Applicants submit that Claims 36 and 37 are not anticipated for the same reasons. In addition, Applicants respectfully submit that Claims 36 and 37 are not anticipated or rendered obvious at least because Fleming *et al.* is entirely silent as to whether the patients to be treated by such a method have a recognized need for the specific treatment of inflammatory bowel disease *that is associated with shortening of intestinal length, loose stool or diarrhea. See Jansen v. Rexall Sundown*, 342 F.3d 1329, 1334 (Fed. Cir. 2003), cited in MPEP 2111.02 II. The issue is not whether the antibody of Fleming *et al.* would inherently treat inflammatory bowel disease (IBD) associated with shortening of intestinal length, loose stool or diarrhea -if attempted- as the rejection posits, but rather, whether Fleming *et al.* *discloses* the treatment of inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea. Such is not disclosed in Fleming *et al.* Thus, Fleming *et al.* does not anticipate Claims 36 and 37 for this reason also.

Withdrawal of the rejection is respectfully requested.

2. On page 5 of the Office Action, Claims 19, 20, 31, 32 and 35 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Curd *et al.* (WO 00/67796), essentially for reasons of record.

Specifically, the Examiner contends that Curd *et al.* teaches a method for treating inflammatory bowel disease, comprising administering an anti-CD81 antibody, citing Claims 1, 2, 3, 6 and 7. Although the Examiner acknowledges that Curd *et al.* is entirely silent as to the treatment, or improvement, of shortened intestinal length or diarrhea, the Examiner considers such properties to be inherent in the disclosure of Curd *et al.*

In response to Applicants' previous arguments that the rejection is predicated on impermissible picking and choosing, and that Curd *et al.* does not disclose the presently claimed method with "sufficient specificity" to establish anticipation, the Examiner contends that such arguments are unpersuasive. The Examiner alleges that it is "immediately apparent" that there is no need for picking or choosing because "all the diseases listed by Curd *et al.* … are linked by the B-cell surface marker such as CD81 and being autoimmune diseases such as inflammatory bowel disease." (Emphasis added.) Moreover, the Examiner contends that the relied-upon claims, which disclose 25 B-cell surface markers, and 65 autoimmune diseases, disclose a "very small genus of diseases and B-cell surface markers" sufficient to anticipate.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully submit that the rejection over Curd *et al.* is improper at least for the reasons set forth above in response to the rejection over Fleming *et al.* Indeed, Applicants note that arriving at the claimed invention from the disclosure of Curd *et al.* requires, as a predicate, first choosing CD81 from the myriad B-cell markers recited in the claims, then

selecting the treatment of inflammatory bowel disease. Like Fleming *et al.*, nothing in Curd *et al. directs* those of ordinary skill in the art to the combination of elements claimed by Applicants.

Nor is this a case where Curd *et al.* discloses such a limited genus that the specific method claimed by Applicants is disclosed with "sufficient specificity," as the law requires. Even assuming *arguendo* that the genera of B-cell markers and diseases, when considered individually are limited, Applicants note that the relevant genus in Curd *et al.* is the methods disclosed by the combinations of these genera. That is, Claims 2 and 6, taken in combination as the Examiner has done, disclose a genus of 1625 distinct methods, without disclosing any particular species thereof. Applicants respectfully disagree that this constitutes a sufficiently limited genus to compel a finding of anticipation, particularly in view of governing law.

For example, in *In re Petering*, 301 F.2d 676 (C.C.P.A. 1962), the court acknowledged that although a broad genus was disclosed by the allegedly anticipatory reference, the reference identified "specific preferences" which served to narrow the broad disclosure to just a small number of species, of which the later-described species fell within. The court held that this narrow genus of compounds, defined by these "specific preferences," were so few in number (only 22 species) that all the species therein were sufficiently described so as to anticipate those species. Similarly, in *In re Schaumann*, 572 F.2d 312 (C.C.P.A. 1978), the court found that a prior art patent disclosed a limited class of compounds based on a disclosed "preference" for the one variable substituent. The court concluded that the compound in the rejected claim fell within the scope of that limited class of compounds, and thus was anticipated by the prior art patent. Thus, without a pattern of "specific preferences" that serve to narrow a broad disclosed genus to a small number of species, a finding of anticipation is improper. Unlike the prior art at issue in *Petering* and *Schaumann*, Curd *et al.* fails to disclose or suggest any pattern of preferences that

would serve to narrow the broad genus of possible methods encompassed by the claims therein to a small number of species that encompasses Applicants' claimed method. To the contrary, the "pattern of preferences" within Curd *et al.* is not for an antagonist of CD81, but for an antagonist of CD19 or CD20.

Moreover, Applicants respectfully submit that the rejection is also improper because it would require an extensive and undue amount of experimentation for those of skill in the art to specifically link CD81 with inflammatory bowel disease, because Curd *et al.* provides insufficient direction. Relevant law indicates that prior art containing broad disclosures of alternatives is non-enabling, and thus not anticipatory, where so little guidance is provided to direct those of skill in the art to the later-claimed combination. *See, e.g., Impax Laboratories, Inc. v. Aventis Pharmaceuticals, Inc.*, 545 F.3d 1312 (Fed. Cir. 2008). In *Impax*, the district court held that because the alleged prior art disclosed hundreds of compounds, and several diseases, but did not provide any disclosure that would have directed those of ordinary skill in the art to recognize that riluzole could be used to treat ALS, it would have required "extensive experimentation to link riluzole with the treatment of ALS [the subject matter of the claim at issue]." Similarly, in the instant case, it would require an extensive and undue amount of experimentation for those of skill in the art to have to specifically linked CD81 with inflammatory bowel disease, based on the mere listing of these elements within broad lists of myriad alternatives, because Curd *et al.* provides no direction or guidance that would lead those of skill in the art to the claimed method. As noted above, Curd *et al.* directs those of skill in the art to CD19 or CD20, not CD81. Thus, Curd *et al.* does not enable the claimed invention, and thus is not anticipatory.

Applicants submit that Claims 36 and 37 are not anticipated for the same reasons. In addition, Applicants respectfully submit that Claims 36 and 37 are not anticipated or rendered obvious at least because Curd *et al.* is entirely silent as to whether the patients to be treated by such a method have a recognized need for the specific treatment of inflammatory bowel disease *that is associated with shortening of intestinal length, loose stool or diarrhea. See Jansen v. Rexall Sundown*, 342 F.3d 1329, 1334 (Fed. Cir. 2003), cited in MPEP 2111.02 II. The issue is not whether the antibody of Curd *et al.* would inherently treat inflammatory bowel disease (IBD) associated with shortening of intestinal length, loose stool or diarrhea -if attempted- as the rejection posits, but rather, whether Curd *et al. discloses* the treatment of inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea. Such is not disclosed in Curd *et al.* Thus, Curd *et al.* does not anticipate Claims 36 and 37 for this reason also.

Withdrawal of the rejection is respectfully requested.

Claims 19, 20 and 31-35 are Patentable Under 35 U.S.C. § 103(a)

1. On page 6 of the Office Action, Claims 31, 33 and 34 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over any of U.S. Patent No. 6,423,501, WO 98/25647 or WO 00/67796, in view of Owens *et al.* (*Journal of Immunol. Methods*, 1994, 68:149-165).

In making the rejection, the Examiner relies upon Fleming *et al.*, WO 98/25647 and WO 00/67796 for the same reasons as in the anticipation rejections discussed above. However, the Examiner acknowledges that neither Fleming *et al.*, WO 98/25647 nor WO 00/67796 disclose or suggest using a Fab, $F(ab')_2$, Fv or scFv, as recited in Claim 31. In an attempt to rectify such

deficiency, the Examiner cites to Owens *et al.*, who allegedly discloses the production of single chain antibodies, Fab fragments, and $F(ab')_2$ fragments. The Examiner contends that one of ordinary skill in the art would readily have modified the antibodies of Fleming *et al.*, WO 98/25647 or WO 00/67796 to produce such antibody molecule variants, because they are "the reagents of choice for some clinical applications." Further, the Examiner contends that one of ordinary skill in the art would readily have arrived at the claimed dosages in Claims 33 and 34 through routine optimization.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

As previously noted on the record, and as discussed above, neither Fleming *et al.*, WO 98/25647 nor WO 00/67796 disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in these references that would incite any expectation of success in performing such a method. Owens *et al.* fails to rectify this deficiency, being silent as to CD81 and inflammatory bowel disease. Thus, even assuming *arguendo* these references were combined, those of ordinary skill in the art would not arrive at the presently claimed invention.

Withdrawal of the rejection is respectfully requested.

2. On page 8 of the Office Action, Claims 19, 20 and 31-35 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fleming *et al.* (U.S. Patent No. 6,423,501 or WO 98/25647).

The Examiner relies upon Fleming *et al.* for essentially the same reasons as discussed above in the outstanding anticipation rejection. However, the Examiner appears to assert that Fleming *et al.* does not exemplify treatment *in a patient*.

In justifying the rejection, the Examiner contends that those of ordinary skill in the art would readily have performed such method in a patient, and would have possessed at least a reasonable expectation in doing so, because "[Fleming *et al.*] discloses that such agents are suitable to treat inflammatory responses associated with disorders … [and] discloses two specific examples of … anti-CD-81 antibodies."

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

As previously noted on the record, and as discussed above, Fleming *et al.* does not disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Fleming *et al.* that would incite any expectation of success in performing such a method. Applicants respectfully submit that the presently claimed invention is non-obvious, and patentable, for at least this reason.

Withdrawal of the rejection is respectfully requested.

3. On page 9 of the Office Action, Claims 19-35 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 00/67796 to Curd *et al.*

The Examiner relies upon Curd *et al.* for essentially the same reasons as discussed above in the outstanding anticipation rejection. However, the Examiner appears to assert that Curd *et al.* does not exemplify treatment *in a patient.*

To justify the rejection the Examiner relies on several rationales which are alleged to find basis in the Supreme Court's decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (2007). Essentially, the underlying contention behind each rationale is that Applicants' invention is merely a predictable combination, yielding nothing more than predictable results, and as such would readily have been contemplated by those of ordinary skill in the art.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

As previously noted on the record, and as discussed above, Curd *et al.* does not disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Curd *et al.* that would incite any expectation of success in performing such a method. Applicants respectfully submit that the presently claimed invention is non-obvious, and patentable, for at least this reason.

Withdrawal of the rejection is respectfully requested.

4. On page 12 of the Office Action, Claim 31 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fleming *et al.* (U.S. Patent No. 6,423,501 or WO 98/25647) in view of Owens *et al.* ((*Journal of Immunol. Methods*, 1994, 68:149-165)).

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

As discussed above, Fleming *et al.* does not disclose, either expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Fleming *et al.* that would incite any expectation of success in performing such a method. Owens *et al.* fails to rectify this deficiency, being silent as to CD81 and inflammatory bowel disease. Thus, even assuming *arguendo* these references were combined, those of ordinary skill in the art would not arrive at the presently claimed invention.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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